Optical, chemical, and biochemical sensors in medicine

Francesco Baldini

The development of optical multiarray biochips, essential for the immediate rapid screening of patients, is just one of many emerging (bio)chemical sensing applications.

Optical-chemical and biochemical sensing is being researched extensively all over the world, and these sensors are finding an increasing number of applications in industry, environmental monitoring, medicine, biomedicine, and chemical analysis. The main physical phenomena exploited for optical chemical sensing are absorption and fluorescence, although chemical luminescence, Raman scattering, and plasmon resonance have also been used. Optical sensors are mainly based on amplitude-modulation: the intensity of the light is directly modulated by the parameter being investigated (which has optical properties) or by a chemical transducer whose optical properties vary with the concentration of the parameter under study. In the case of fluorescence, time- or phase-modulation is often preferred to amplitude-modulation, since sensor response is practically unaffected by the photobleaching of the chemical transducer in the latter case.

Health-care is unquestionably the application field which seems to have the most potential for future development. Optical biosensors are finding ever-increasing applications in different branches of medicine for several reasons.

Invasive sensors
First of all, miniaturization (by using optical fibers, for instance) can make it possible to directly measure biomedical parameters by allowing the probe to be placed either in contact with human skin or inside the body. Optical catheters with diameters of the order of dozens of microns, and probe heads miniaturized to a few microns, enable physicians to arrive at places inside the human body that would be unthinkable with other sensor technologies.

In collaboration with Joanneum Research (Graz, Austria), we have developed an optical fiber sensor for the continuous monitoring of carbon-dioxide partial pressure in the stomach. The sensor is based on the color change of a CO₂-sensitive indicator layer. This layer is attached to the distal end of an optical fiber positioned in the stomach or in the oesophagus. The optoelectronic unit is connected to a laptop that is used for data acquisition and processing, and for calibration (see Figure 1).

Another example of the potential of optical sensors in biomedicine is the development of an intelligent system for improved monitoring of critically ill patients. This is the aim of the four-year EU-funded project CLINICIP (Closed Loop Insulin Infusion for Critically Ill Patients) that began in 2004. The system under development includes optical sensors for the determination of glucose, pH, pO₂ and pCO₂. Microdialysis is used to extract samples from either the subcutaneous adipose tissue or blood: the drawn sample flows through a microfluidic circuit formed by the microdialysis catheter in line with the sensors, with the chemical transducers on the internal walls of the glass capillaries.

Continued on next page
Figure 2. Sketch of the working principle of a microcantilever-based chemical sensor. A single cantilever is typically 500μm long and 200μm wide. Displacements of the order of few nanometers can be detected.

Sensor arrays

Another important possibility for clinical diagnostics is the development of multiarray biochips for the analysis of multiple parameters in parallel. Not only are these essential for immediate rapid screening of the patient, but they also offer physicians the right tool for correct and rapid diagnosis.

High-density optical microarray platforms have already been developed: thousands of 50–100μm spots have been deposited on glass slides or on microliter plate wells, each of which carry a different chemistry for the detection of different parameters. A high-density optical fiber microarray platform has also been developed: this uses a 1mm-diameter optical fiber bundle that contains 50,000 individually-addressable 3μm-diameter fibers.

Novel approaches

Two new approaches have recently been proposed: a ‘mechanical’ approach, based on the use of microcantilever sensors, and a resonant approach, in which the optical interaction takes place in a resonant microcavity.

The use of microcantilevers as transducers for chemical and biochemical sensing has only become widespread in the last few years, mainly due to their use in the development of microsensor arrays. However, the invention of scanning-force microscopy, in which the microcantilever plays the fundamental role of force transducer, goes back to the 1980s. The idea is quite simple: the surface of the cantilever, a rectangular thin beam clamped at one end, is chemically modified so that it can react with specific compounds. The mass deposition that follows the chemical reaction causes a stress, and this leads to a detectable bending of the cantilever (see Figure 2). Recent work has shown the capability of these micromechanical structures to investigate DNA hybridization and antibody-antigen recognition.

In terms of resonance, dielectric microspheres with diameters in the 50–300μm range are used as optical cavities. The principle is based on the frequency shift of the resonance modes caused by adsorption/binding of the chemicals under investigation on the surface of the microspheres (see Figure 3). For a silica-glass microsphere with a diameter of 200μm, the distance the resonant wave covers is roughly 20m; the light mode circumnavigates the equator roughly 60,000 times. This potentially makes the approach very sensitive, since the light interacts with the external medium along a very great distance. From a theoretical point of view, even single-protein detection is possible.

Conclusions

Optical sensors are under continuous development and offer physicians reliable and efficient tools for diagnoses. The instruments already available on the market, and the many systems now at advanced stage in labs, demonstrate that optical sensors are some of the best options for scientists and physicians when in-vivo continuous monitoring is necessary.

Author Information

Francesco Baldini
Institute of Applied Physics
Firenze, Italy

Continued on next page
Dr Francesco Baldini graduated with a magna cum laude degree in physics from the University of Florence in 1986. His research has been devoted to the development of optical sensors and to the application of optical methods to the restoration of paintings. He is currently active in the field of optical sensors/systems for chemical and biochemical parameters. He is author of more than 80 publications on the subject in international journals, scientific books, and at international conference. In addition, he has been conference chair/co-chair of many SPIE conferences, including Biomedical Optics Europe and the Photonics East symposium. He has been an invited speaker at many SPIE conferences and published in many SPIE proceedings.

References